Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

These amendments introduce no new matter and support for the amendment is replete throughout the specification and claims as originally filed. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter, or agreement with any objection or rejection of record.

Listing of Claims:

1. (Currently Amended) A method of selecting a polypeptide that is internalized into a target cell, said method comprising:

i) contacting one or more target cells with one or more members of a phage display library displaying one or more polypeptides;

ii) ~~washing said target cells to remove and eliminate members of said library that are bound to the exterior surface of said target cells, wherein said washing comprises washing said target cells with a strong wash;~~

~~iii)~~ culturing ~~said~~ the one or more target cells and enriching internalized library members under conditions where said internalized library members of said phage display library ~~bound to an internalizing marker can be internalized~~are enriched at least 30-fold as compared to non-internalized library members; and

~~iv)~~ iii) identifying internalized library members of said phage display library ~~that are internalized into one or more of said target cells~~, thereby selecting for a polypeptide that is internalized into the target cell.

2. (Original) The method of claim 1, wherein said phage display library is an antibody phage display library.

3. (Original) The method of claim 2, wherein said antibody phage display library displays single chain antibody Fv regions.

4. (Currently amended) The method of claim 1, wherein said identifying comprises recovering internalized phage and repeating steps (i) through ~~(iv)~~(iii) to further select for internalizing binding moieties.

5. (Original) The method of claim 4, wherein said recovering comprises: (a) lysing said target cells to release internalized phage; and (b) infecting a bacterial host with said internalized phage to produce phage for a subsequent round of selection.

6. (Original) The method of claim 4, wherein said recovering comprises recovering nucleic acids encoding the phage-displayed antibody.

7. (Original) The method of claim 1, wherein said identifying comprises detecting expression of a reporter gene or a selectable marker.

8. (Previously presented) The method of claim 51, wherein said cells of a subtractive cell line are present in at least 2-fold excess over said target cells.

9. (Original) The method of claim 1, wherein said target cells form an adherent layer in said method.

10. (Cancelled) ~~The method of claim 1, wherein step (ii) is performed at a temperature lower than step (iv).~~

11. (Cancelled) ~~The method of claim 1, wherein step (ii) comprises a wash performed at about 4° C.~~

12. (Original) The method of claim 1, wherein said phage express a selectable marker.

13. (Original) The method of claim 12, wherein said selectable marker is selected from the group consisting of a fluorescent protein, an antibiotic resistance gene, and a chromagenic gene.

14. (Original) The library of claim 13, wherein said chromagenic gene is selected from the group consisting of horse radish peroxidase, B-lactamase, luciferase, and B- galactosidase.

15. (Original) The method of claim 1, wherein said target cells are selected from the group consisting of solid tumor cells, members of a cDNA expression library, cells

that overexpress a cytokine receptor, cells that overexpress a growth factor receptor, metastatic cells, cells of a transformed cell line, cells transformed with a gene or cDNA encoding a specific surface target receptor, and neoplastic cells derived from outside a solid tumor.

16. (Previously presented) The method of claim 51, wherein said cells of a subtractive cell line are selected from the same tissue type as the target cells.

17. (Previously presented) The method of claim 51, wherein said cells of a subtractive cell line are selected from the group consisting of fibroblasts, monocytes, stem cells, and lymphocytes.

51. (Currently Amended) The method of claim 1, wherein said method further comprises contacting the ~~target cells~~ members of the phage display library with cells of a subtractive cell line.

52. (Currently Amended) The method of claim 51, wherein said method further comprises contacting the ~~target cells~~ members of the phage display library with live cells of a subtractive cell line.

53. (Currently Amended) The method of claim 1, wherein ~~said removing~~ culturing said target cells and enriching internalized library members comprises contacting the target cells with a low pH wash.

54. (Currently Amended) The method of claim 51, wherein ~~said removing~~ culturing said target cells and enriching internalized library members comprises contacting the target cells with a low pH wash.

55. (Currently Amended) The method of claim 1, wherein ~~said removing comprises contacting the target cells with a trypsin.~~ culturing said target cells and enriching internalized library members comprises trypsinizing the target cells

56. (Currently Amended) The method of claim 51, wherein ~~said removing comprises contacting the target cells with a trypsin.~~culturing said target cells and enriching internalized library members comprises trypsinizing the target cells

57. (Previously presented) The method of claim 51, wherein the target cells are cells that are transformed a nucleic acid that encodes and expresses a target receptor and the subtractive cell line is the non-transformed cell line.

58. (New) A method of selecting a polypeptide that is internalized into a target cell, comprising:

i) contacting one or more target cells with one or more members of a phage display library displaying one or more polypeptides;

ii) culturing the one or more target cells under conditions wherein members of said phage display library bound to an internalizing marker become internalized;

iii) reducing non-internalized members of said phage display library by removing phage trapped in an extracellular matrix; and

iv) identifying members of said phage display library that are internalized into one or more of said target cells, where the internalized library members of said phage display library each display a polypeptide that is internalized into a target cell.

59. (New) The method of claim 58, wherein removing the phage trapped in the extracellular matrix comprises washing the one or more target cells with a stripping buffer comprising 50 mM glycine pH 2.8, 0.5 M NaCl, 2M urea, and 2% polyvinylpyrrolidone.

60. (New) The method of claim 58, wherein removing the phage trapped in the extracellular matrix comprises trypsinizing the one or more target cells.

61. (New) The method of claim 58, wherein said phage display library is an antibody phage display library.

62. (New) The method of claim 61, wherein said antibody phage display library displays single chain antibody Fv regions.

63. (New) The method of claim 58, wherein identifying the internalized library members comprises recovering internalized phage and repeating steps (i) through (iv) to further select for internalizing binding moieties.

64. (New) The method of claim 63, wherein said recovering comprises: (a) lysing said target cells to release internalized phage; and (b) infecting a bacterial host with said internalized phage to produce phage for a subsequent round of selection.

65. (New) The method of claim 63, wherein said recovering comprises recovering nucleic acids encoding the phage-displayed antibody.

66. (New) The method of claim 58, wherein identifying the internalized library members comprises detecting expression of a reporter gene or a selectable marker.

67. (New) The method of claim 58, wherein said target cells form an adherent layer in said method.

68. (New) The method of claim 58, wherein said phage express a selectable marker.

69. (New) The method of claim 68, wherein said selectable marker is selected from the group consisting of a fluorescent protein, an antibiotic resistance gene, and a chromagenic gene.

70. (New) The library of claim 69, wherein said chromagenic gene is selected from the group consisting of horse radish peroxidase, B-lactamase, luciferase, and B- galactosidase.

71. (New) The method of claim 58, wherein said target cells are selected from the group consisting of solid tumor cells, members of a cDNA expression library, cells that overexpress a cytokine receptor, cells that overexpress a growth factor receptor, metastatic cells, cells of a transformed cell line, cells transformed with a gene or cDNA encoding a specific surface target receptor, and neoplastic cells derived from outside a solid tumor.

72. (New) The method of claim 58, wherein said method further comprises contacting the members of the phage display library with cells of a subtractive cell line.

73. (New) The method of claim 72, wherein said cells of a subtractive cell line are selected from the same tissue type as the target cells.

74. (New) The method of claim 72, wherein said cells of a subtractive cell line are selected from the group consisting of fibroblasts, monocytes, stem cells, and lymphocytes.

75. (New) The method of claim 72, wherein said cells of a subtractive cell line are present in at least 2-fold excess over said target cells.

76. (New) The method of claim 72, wherein said cells of a subtractive cell line are live cells.

77. (New) The method of claim 72, wherein the target cells are cells that are transformed a nucleic acid that encodes and expresses a target receptor and the subtractive cell line is the non-transformed cell line.

Applicants respectfully request that the amendments to the claims be entered.